

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3022	Cell (graft OR implant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:00
L2	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:00
L3	51	l1 and L2	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:02
L4	2	("5759830").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/09/02 11:09
L5	3	((("6068837") or ("5645829")).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/09/02 11:09
S1	29	Donahoe patricia	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:25
S2	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:44
S3	12910	cell matrix	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:26
S4	157	S2 and S3	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:26
S5	29	mullerian inhibiting substance.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:49
S6	1	S5 and gene therapy	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51
S7	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51
S8	419	S7 and gene therapy	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51

S9	376	S8 and (matrix polymer)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:52
S10	37	S8 and (matrix polymer).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:53
S11	133	S9 and (graft implant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:56

=> d his

(FILE 'HOME' ENTERED AT 11:19:46 ON 02 SEP 2005)

FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT
11:20:07 ON 02 SEP 2005

L2 1660 S MULLERIAN INHIBITING?
L3 8 S L2 AND (GENE THERAPY)
L4 8 DUP REM L3 (0 DUPLICATES REMOVED)
L5 294145 S CELL (L) (TRANSPLANT? OR IMPLANT?)
L6 30 S L2 (L) L5
L7 13 DUP REM L6 (17 DUPLICATES REMOVED)
L8 13 SORT L7 PY
L9 1089271 S MATRIX OR SCAFFOLD OR HYDROGEL? OR BIOAMATRI?
L10 23 S L2 (L) L9
L11 15 DUP REM L10 (8 DUPLICATES REMOVED)
L12 15 SORT L11 PY
E DONAHOE PATRICIA?/AU
L13 184 S E2
E MACLAUGHLIN DAVID?/AU
L14 85 S E2
L15 89 S L13 AND L2
L16 43 S L14 AND L2
L17 95 S L16 OR L15
L18 81 DUP REM L17 (14 DUPLICATES REMOVED)
L19 4 S L18 AND L5
L20 2 S L18 AND L9
L21 4 S L19 OR L20
L22 4 DUP REM L21 (0 DUPLICATES REMOVED)

=> d an ti so au ab pi l22 1-4

L22 ANSWER 1 OF 4 MEDLINE on STN
AN 2002425819 MEDLINE
TI Highly purified **mullerian inhibiting** substance
inhibits human ovarian cancer in vivo.
SO Clinical cancer research : an official journal of the American Association
for Cancer Research, (2002 Aug) 8 (8) 2640-6.
Journal code: 9502500. ISSN: 1078-0432.
AU Stephen Antonia E; Pearsall Lisa A; Christian Benjamin P; **Donahoe**
Patricia K; Vacanti Joseph P; **MacLaughlin David T**
AB PURPOSE: **Mullerian inhibiting** substance (MIS) causes
Mullerianduct regression in mammalian, avian, and reptilian embryos; MIS
also inhibits growth in vitro of Mullerian-derived **cell** lines
and primary **cells** from human ovarian carcinomas. We hypothesize
that highly purified MIS delivered parenterally inhibits ovarian cancer in
vivo. EXPERIMENTAL DESIGN: To test the efficacy of highly purified MIS
against ovarian cancer **cell** lines in vivo, we treated
immunosuppressed mice with MIS after **implanting** OVCAR 8 or IGROV
1 human ovarian cancer **cells** beneath the renal capsules and
measured tumor volume over time. Animals were treated with daily
injections of 10 micro g of purified exogenous recombinant human MIS or by
endogenous MIS secreted from **cells** growing on biodegradable
mesh. RESULTS: The average graft size ratio (change in size compared with
starting size) of the OVCAR 8 tumor **implants** was larger in the
control animals than in animals treated for 2 weeks (P < 0.019) or 3 weeks
(P < 0.001) with parenteral MIS, or after treating with MIS produced from
transfected **cells**, which impregnated the biodegradable mesh (P =
0.02). The average graft size ratio of the IGROV 1 tumors was also larger
in the control animals than in those treated with injected MIS (P =
0.0174). CONCLUSIONS: Highly purified recombinant human MIS, delivered
parenterally, or MIS produced endogenously causes inhibition of human
ovarian cancer **cell** lines in vivo, providing convincing
preclinical evidence to support the use of MIS as a parenteral agent for
the treatment of ovarian cancer.

L22 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:565104 CAPLUS
DN 135:127275

TI Delivery of therapeutic biological from implantable tissue matrices

SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

IN Vacanti, Joseph P.; Donahoe, Patricia K.; MacLaughlin, David T.; Masiakos, Peter T.

AB Normal cells, such as fibroblasts or other tissue or organ cell types, are genetically engineered to express biol. active, therapeutic agents, such as proteins that are normally produced in small amts., for example, MIS (Mullerian inhibiting substance), or other members of the TGF-beta family HerceptinTM, interferons, and anti-angiogenic factors. These cells are seeded into a matrix for implantation into the patient to be treated. Cells may also be engineered to include a lethal gene, so that implanted cells can be destroyed once treatment is completed. Cells can be implanted in a variety of different matrixes. In a preferred embodiment, these matrixes are implantable and biodegradable over a period of time equal to or less than the expected period of treatment, when cells engraft to form a functional tissue producing the desired biol. active agent. Ovarian cancer cell lines that were responsive to MIS in vitro were place beneath th renal capsules of mice. CHO B9 cells seeded onto a polyglycolic acid matrix and were implanted in the mice. MIS produced by th B9 cells significantly inhibited the growth of the human ovarian cancer cell line in vivo.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 2001055212	A2	20010802	WO 2001-US2694	20010126
WO 2001055212	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

L22 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:222623 CAPLUS

DN 135:29396

TI Tissue-engineered cells producing complex recombinant proteins inhibit ovarian cancer in vivo

SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(6), 3214-3219

CODEN: PNASA6; ISSN: 0027-8424

AU Stephen, Antonia E.; Masiakos, Peter T.; Segev, Dorry L.; Vacanti, Joseph P.; Donahoe, Patricia K.; MacLaughlin, David T.

AB Techniques of tissue engineering and cell and mol. biol. were used to create a biodegradable scaffold for transfected cells to produce complex proteins. Mullerian Inhibiting Substance (MIS) causes regression of Mullerian ducts in the mammalian embryo. MIS also causes regression in vitro of ovarian tumor cell lines and primary cells from ovarian carcinomas, which derive from Mullerian structures. In a strategy to circumvent the complicated purification protocols for MIS, Chinese hamster ovary cells transfected with the human MIS gene were seeded onto biodegradable polymers of polyglycolic acid fibers and secretion of MIS confirmed. The polymer-cell graft was implanted into the right ovarian pedicle of severe combined immunodeficient mice. Serum MIS in the mice rose to supraphysiol. levels over time. One week after implantation of the polymer-cell graft, IGROV-1 human tumors were implanted under the renal capsule of the left kidney. Growth of the IGROV-1 tumors was significantly inhibited in the animals with a polymer-cell graft of MIS-producing cells, compared with controls. This novel MIS delivery system could have broader applications for other inhibitory agents not amenable to efficient purification and provides in vivo evidence for a role of MIS in the treatment

of ovarian cancer.

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:144219 CAPLUS

DN 116:144219

TI Recombinant human **Mullerian inhibiting** substance
inhibits human ocular melanoma cell lines in vitro and in vivo
SO Cancer Research (1992), 52(5), 1182-6
CODEN: CNREA8; ISSN: 0008-5472

AU Parry, Robert L.; Chin, Taiwai; Epstein, James; Hudson, Peter L.; Powell,
David M.; Donahoe, Patricia K.

AB Since **Mullerian Inhibiting** Substance (MIS) causes
regression of the Mullerian duct, the anlagen of the uterus, vagina, and
fallopian tube, it was expected and previously observed that purified
recombinant human MIS causes regression of gynecol. tumors. However,
recent expts. indicating that neural crest derivs. might be responsive to
MIS prompted study of a group of human ocular melanoma **cell**
lines in 4 in vitro inhibition assays, and a subrenal capsule assay in
vivo. Ocular melanoma **cell** lines that grew well in a resp.
assay were studied with MIS to determine whether this biol. modifier could
inhibit growth. Three human ocular melanomas, OM431, OM467, and OM482,
were growth-inhibited by highly purified human recombinant MIS in soft
agarose. A dose-dependent tumor inhibition was noted when OM431
cells were incubated with MIS in a liquid colony inhibition assay.
In addition, OM467 was inhibited by MIS in a multicellular tumor spheroid
assay. Cell cycle anal. indicated that OM431 **cells**
were inhibited in monolayer by MIS while in G1. At 100-fold lower serum
concns. than required in the media of in vitro assays, MIS delivered via
i.p. osmotic pumps inhibited in vivo the growth of OM431 **implanted**
beneath the renal capsule of nude and CD-1 irradiated mice when compared
to mice given **implants** of pumps containing no MIS. The
responsiveness of ocular melanoma to MIS broadens the spectrum of tumors
that might be treated with MIS and suggests further investigation of other
neural crest tumors.